

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Reissue Application of U.S. Patent No.: 5,369,108 Issue Date: November 29, 1994

For: POTENT INDUCERS OF TERMINAL DIFFERENTIATION
AND METHODS OF USE THEREOF

Date: 11/2/01

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PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.173

Box REISSUE
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

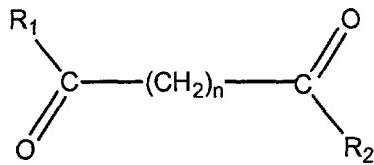
This Preliminary Amendment is submitted as part of the above-referenced Reissue Application. Amendments to the claims are made in accordance with to 37 C.F.R. §§ 1.173(b)(2) and 1.173(d)(2). The requisite fees are being filed concurrently.

Please amend the application as shown below:

In the Claims:

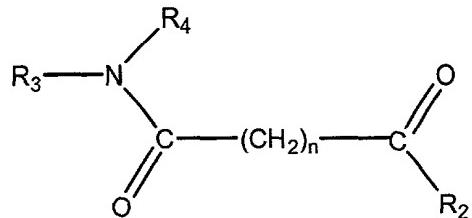
Please amend the claims as shown below:

1. (Amended) A compound having the structure:



wherein [each of R_1 and R_2 are independently the same as or different from each other; when] R_1 and R_2 are the same[,each is] and are a substituted or unsubstituted [cycloalkylamino, pyridineamino, piperidino, 9-purine-6-amine, or] thiazoleamino group; [when R_1 and R_2 are different, $\text{R}_1=\text{R}_3-\text{N}-\text{R}_4$, wherein each of R_3 and R_4 are independently the same as or different from each other and are a hydrogen atom, a hydroxyl group, a substituted or unsubstituted , branched or unbranched alkyl, alkenyl, cycloalkyl, aryl, alkyloxy, aryloxy, arylalkyloxy, or pyridine group, or R_3 and R_4 bond together to form a piperidine group, and R_2 is a hydroxylamino, hydroxyl, amino, alkylamino, or alkyloxy group;] and n is an integer from about 4 to about 8.

2. (Amended) A compound [of claim 1] having the structure:



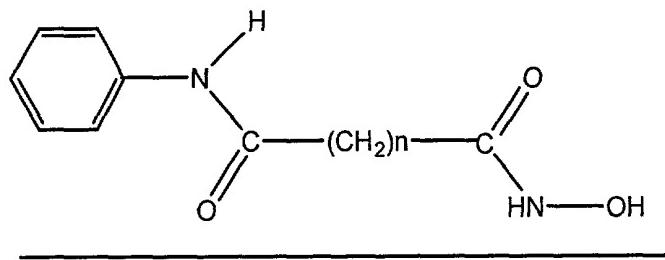
wherein each of R₃ and R₄ are independently the same as or different from each other and are a hydrogen atom, a hydroxyl group, a substituted or unsubstituted, branched or unbranched alkyl, alkenyl, cycloalkyl, aryl, alkyloxy, aryloxy, arylalkyloxy, or pyridine group, or R₃ and R₄ bond together to form a piperidine group; R₂ is a hydroxylamino[, hydroxyl, amino, alkylamino, or alkyloxy] group; [and] n is an integer from [about 4] 5 to about 8; and R₃-N-R₄ and R₂ are different.

3. (Amended) A compound of claim 2, wherein [R₂ is a hydroxylamino, hydroxyl, amino, methylamino, or methyoxy group and] n is 6.
5. (Amended) A compound of claim 4, wherein the phenyl group is substituted with a methyl, cyano, nitro, trifluoromethyl, amino, aminocarbonyl, methylcyano, chloro, fluoro, bromo, iodo, 2,3-difluoro, 2,4-difluoro, 2,5-difluoro, 3,4-difluoro, 3,5-difluoro, 2,6-difluoro, 1,2,3-trifluoro, 2,3,6-trifluoro, 2,4,6-trifluoro, 3,4,5-trifluoro, 2,3,5,6-tetrafluoro, 2,3,4,5,6-pentafluoro, azido, hexyl, t-butyl, phenyl, carboxyl, hydroxyl, [methyoxy] methoxy, phenoxy, benzyloxy, phenylaminoxy, phenylaminocarbonyl, [methoxycarbonyl] methoxycarbonyl, methylaminocarbonyl, dimethylamino, dimethylaminocarbonyl, or hydroxylaminocarbonyl group.
7. (Amended) A compound of claim 3, wherein R₄ is a hydrogen atom and R₃ is a [methyoxy] methoxy group.
11. (Amended) A compound of claim [3] 2, wherein R₄ is a hydrogen atom and R₃ is a [δ -pyridine] γ -pyridine group.
12. (Amended) A compound of claim [3] 2, wherein R₄ is a hydrogen atom and R₃ is a β -pyridine group.

13. (Amended) A compound of claim [3] 2, wherein R₄ is a hydrogen atom and R₃ is a α-pyridine group.

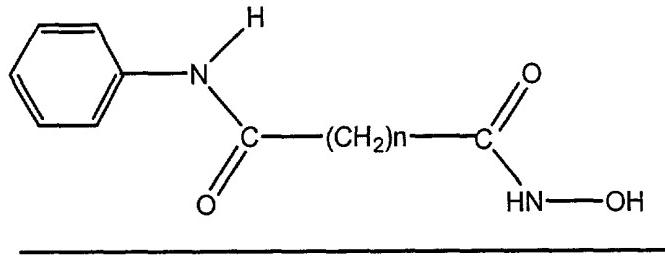
Please add Claims 18-29.

18. A compound having the structure:



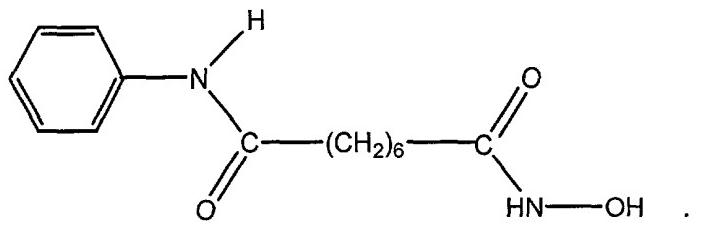
wherein n is an integer from 5 to about 8.

19. A pharmaceutical composition comprising a therapeutically effective amount of a compound having the structure:

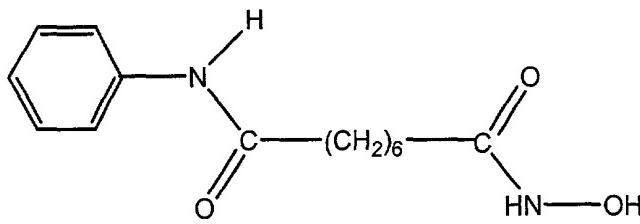


wherein n is an integer from 5 to about 8;
and a pharmaceutically acceptable carrier.

20. A compound having the structure:

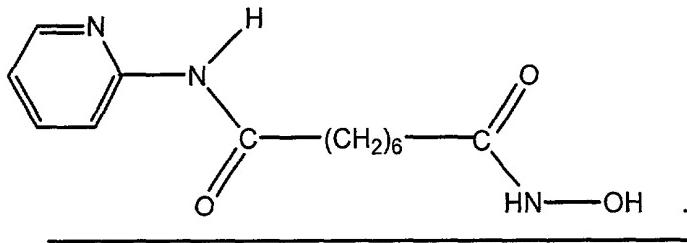


21. A pharmaceutical composition comprising a therapeutically effective amount of a compound having the structure:

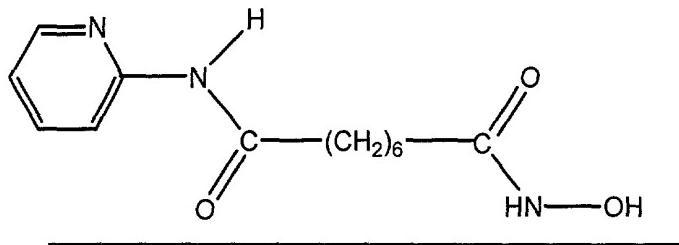


and a pharmaceutically acceptable carrier.

22. A compound having the structure:

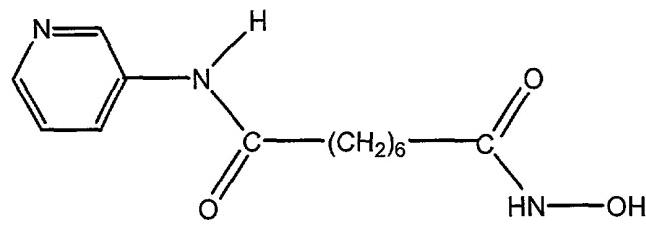


23. A pharmaceutical composition comprising a therapeutically effective amount of a compound having the structure:

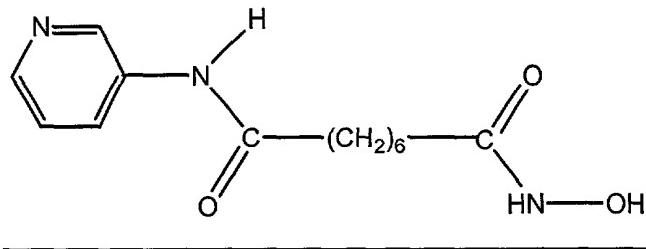


and a pharmaceutically acceptable carrier.

24. A compound having the structure:

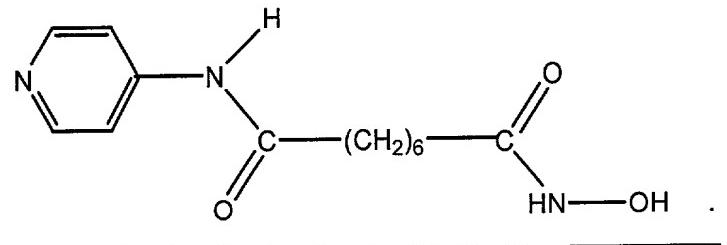


25. A pharmaceutical composition comprising a therapeutically effective amount of a compound having the structure:

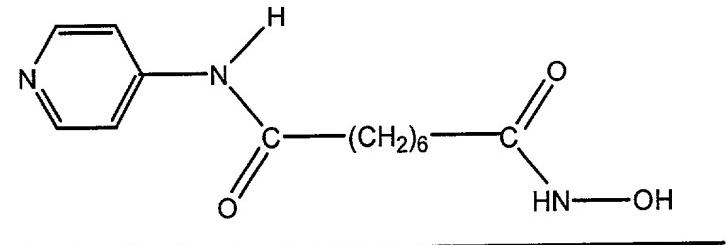


and a pharmaceutically acceptable carrier.

26. A compound having the structure:

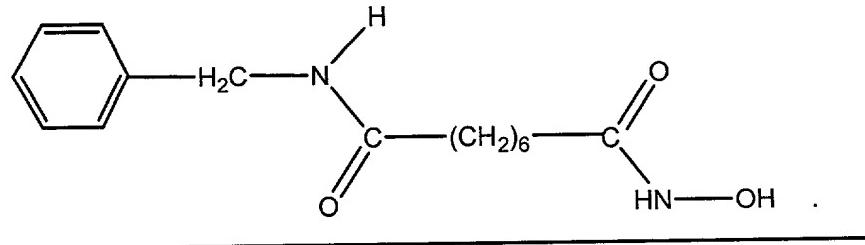


27. A pharmaceutical composition comprising a therapeutically effective amount of a compound having the structure:

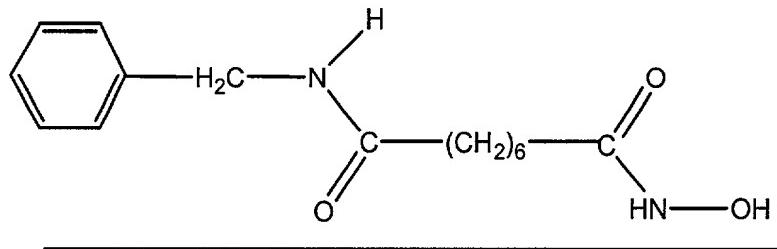


and a pharmaceutically acceptable carrier.

28. A compound having the structure:



29. A pharmaceutical composition comprising a compound having the structure:



and a pharmaceutically acceptable carrier.

REMARKS

Claim 1 has been amended to recite that R₁ and R₂ of the structure set forth in the claim are the same and are a substituted or unsubstituted thiazoleamino group. Support for this amendment can be found, *inter alia*, in the originally issued claims and at Col. 7, lines 40-52 of the specification.

Claim 2 has been amended to be in independent form and to recite that R₂ is a hydroxylamino group and is different from R₃-N-R₄ as shown in the formula. In addition, the definition of n has been amended to recite that n is an integer from 5 to about 8. Support for these amendments can be found, *inter alia*, in the originally issued claims, at Col. 2, line 65-Col. 3, line 6, at Col. 6, line 59-Col. 7, line 7 and in Table 1, as Entries 2-5 of Column "CPD".

Claim 3 has been amended to further define the integer n as 6. Support for this amendment can be found in originally issued Claim 3 and throughout the specification.

Claims 5 and 7 have been amended to correct obvious typographical errors. Support for this amendment can be found, for example, in Table 1, Entries 51-53 and in the art.

Claims 11, 12 and 13 have been amended to depend from Claim 2 rather than Claim 3. In addition, Claim 11 has been amended to designate the pyridine as a gamma pyridine, γ -pyridine, rather than a delta pyridine, δ -pyridine. This is an obvious error, as δ -pyridine cannot be a substituent. Support for this amendment can be found in the structures at Col. 17, lines 55-62 and Col. 18, lines 25-33.

Claims 18-29 are newly added. These claims have been added to more specifically claim particular compounds set forth in the specification. Claim 18 is directed to the compositions of

the structure set forth in the claim, wherein n is from 5 to about 8. Support for Claim 18 can be found, for example, in Table 1 as Entries 2-5. Claim 19 is directed to a pharmaceutical composition comprising a therapeutically effective amount of a compound having the structure set forth in the claim wherein n is from 5 to about 8. Support for Claim 19 can be found, for example, in Table 1 as Entries 2-5 and in the specification at Col. 6, lines 28-31.

Newly added independent Claim 20 is directed to the compound set forth as Entry 3 in Table 1. As such, support for newly added Claim 20 can be found in Table 1 and also at Col. 26, lines 50-68. Newly added independent Claim 21 is directed to a pharmaceutical composition comprising a therapeutically effective amount of the compound set forth as Entry 3 in Table 1 and a pharmaceutically acceptable carrier. As such, support for newly added Claim 21 can be found in Table 1, at Col. 6, lines 28-31 and at Col. 26, lines 50-68 of the specification.

Newly added independent Claim 22 is directed a compound of the general formula set forth, for example, at Col. 6, line 60 and up of the specification, wherein R₂ is a hydroxylamino group, n is 6, R₃ is a γ-pyridine group and R₄ is hydrogen. Support for newly added Claim 22 can be found, *inter alia*, in originally issued Claim 11 and in the structures at Col. 17, lines 55-62 and Col. 18, lines 25-33. Newly added independent Claim 23 is directed to a pharmaceutical composition comprising a therapeutically effective amount of the compound described above with regard to Claim 22 and a pharmaceutically acceptable carrier. Support for newly added Claim 23 can be found, *inter alia*, in originally issued Claim 11, and in the structures at Col. 17, lines 55-62 and at Col. 18, lines 25-33, and at Col. 6, lines 28-31 of the specification.

Newly added independent Claim 24 is directed to a compound of the general formula set forth, for example, at Col. 6, line 60 and up of the specification, wherein R₂ is a hydroxylamino group, n is 6, R₃ is β-pyridine group and R₄ is hydrogen. Support for newly added Claim 24 can be found, *inter alia*, in originally issued Claim 12. Newly added independent Claim 25 is directed to a pharmaceutical composition comprising a therapeutically effective amount of the compound described above with regard to Claim 24, and a pharmaceutically acceptable carrier. Support for newly added Claim 25 can be found, *inter alia*, in originally issued Claim 12 and at Col. 6, lines 28-31 of the specification.

Newly added independent Claim 26 is directed to a compound of the general formula set forth, for example, at Col. 6, line 60 and up of the specification, wherein R₂ is a hydroxylamino

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group, n is 6, R₃ is α -pyridine group and R₄ is hydrogen. Support for newly added Claim 24 can be found, *inter alia*, in originally issued Claim 13. Newly added independent Claim 27 is directed to a pharmaceutical composition comprising a therapeutically effective amount of the compound described above with regard to Claim 26 and a pharmaceutically acceptable carrier. Support for newly added Claim 27 can be found, *inter alia*, in originally issued Claim 13 and at Col. 6, lines 28-31 of the specification.

Newly added independent Claim 28 is directed to the compound set forth as Entry 19 in Table 1. As such, support for newly added Claim 28 can be found in Table 1. Newly added independent Claim 29 is directed to a pharmaceutical composition comprising a therapeutically effective amount of the compound set forth as Entry 19 in Table 1 and a pharmaceutically acceptable carrier. As such, support for newly added Claim 29 can be found in Table 1 and at Col. 6, lines 28-31 of the specification.

In accordance with 37 C.F.R. 1.173 (3)(c), a separate paper containing the status of all claims, as of the date of this Amendment, and an explanation of the support for the changes, as found in the disclosure of the patent for which a Reissue is sought, is being filed concurrently.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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